REMARKS

It is respectfully requested that this application be reconsidered in view of the above amendments and the following remarks and that all of the claims remaining be allowed.

Amendments in the Specification

The title has been amended to recite "Binding Compounds to IL-B50," and the abstract has been amended to recite IL-B50. Support for these recitations can be found throughout this application, for example, at pages 6-9.

Title and Abstract (Paragraphs 3 and 4 of the Office Action)

The Office Action objects to the title and the abstract. In view of the amendments in the title and the abstract, withdrawal of these objections is respectfully requested.

IDS (Paragraph 5 of the Office Action)

The Office Action states that references AE and AH of Applicants' information disclosure statement (IDS) were not found. These references have been submitted or cited in the parent application. For the convenience of the Examiner, a copy of reference AH, from *The Cytokine Handbook*, 3rd ed., is submitted herewith. Applicants are in the process of locating a copy of reference AE (Friend, Sherree Lee, et al., Experimental Hematology, "A thymic stromal cell line supports in vitro development of surface IgM^+ B cells and produces a novel growth factor affecting B and T lineage cells" (1994), pp. 321-328, Vol. 3) and will submit the same when it is available.

Priority (Paragraph 7 of the Office Action)

The present application claims the benefit of the following priority applications:

- U.S. Provisional Application No. 60/101,318 (the '318 application"), filed September 21, 1998;
- U.S. Provisional Application No. 60/131,298, filed April 27, 1999;

- U.S. Application No. 09/399,492, filed September 20, 1999;
- U.S. Application No. 09/963,347, filed September 25, 2001.

However, the Office Action alleges that the utility of the polypeptide consisting SEQ ID NO:2 is only disclosed in U.S. Application No. 09/963,347, filed September 25, 2001. The Office Action thus concludes that the effective filing date of the present application is September 25, 2001. Applicants respectfully disagree for the reasons set forth below.

The Examiner bears the initial burden of showing that a claimed invention lacks patentable utility. See *In re Brana*, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995) ("Only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence.") In the instant case, the Examiner merely states that the utility is only disclosed in U.S. Application No. 09/963,347, without any explanation or evidence. Therefore, the burden is still upon the Examiner to show that the claimed invention lacks patentable utility.

Although Applicants do not bear the burden of proof, to assist the Examiner, Applicants wish to discuss the fact that the '318 application satisfies the utility requirement. Pursuant to the Utility Examination Guidelines, Federal Register 66(4), 1092, 1098 (2001), the requirement for utility is that a specific, substantial and credible utility is disclosed for the claimed invention. Federal Register 66(4), at 1098. Credibility of an asserted specific and substantial utility can be assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record (e.g., test data, affidavits or declarations from experts in the art, patents or printed publications) that is probative of the applicant's assertions. *Id.*

At least one specific, substantial and credible utility has been disclosed in the '318 application. For example, the '318 application discloses that IL-B50 has stimulatory or inhibitory effects on hematopoietic cells, including, e.g., lymphoid cells, such as T-cells, B-cells, natural killer (NK) cells, macrophages, dendritic cells, and hematopoietic progenitors (page 9, lines 9-13 of the

'318 application). The '318 application further discloses that IL-B50 is a short chain cytokine exhibiting sequence similarity to IL-7 (page 12, lines 1-4), that IL-B50 and IL-7 are likely to share similar biological functions (page 12, second paragraph, particularly line 32), and that IL-7 exhibits strong effects on lymphopoietic development and differentiation (page 59, lines 21-22). IL-B50 can be used to isolate its receptor (page 49, lines 5-6 of the '318 application), and it was predicted that IL-B50 would bind to the alpha subunit of the IL-7 receptor along with another subunit (page 49, lines 25-28 of the '318 application). Therefore, a skilled artisan would have understood from the '318 application that IL-B50 has similar functions as IL-7, such as stimulating lymphopoietic development and differentiation, and that IL-B50 and IL-7 are so closely related that their receptors would share a common subunit. These are real-world, specific utilities. The utilities of binding compounds are also disclosed (see, e.g., pages 26-28 of the '318 application).

These asserted utilities are supported by the data disclosed in the present application. For example, it is shown that IL-B50 induces phosphorylation of Stat3 and Stat5 (page 64, lines 13-16), as well as enhances maturation of dendritic cells (page 67) and expansion/ development of T cells (page 68). The IL-B50 receptor has been identified, and it indeed contains the alpha subunit of the IL-7 receptor (pages 63-64). The data thus indicate that IL-B50 is a hematopoietic cytokine most closely related to IL-7 (page 68, lines 25-26 of the present application) which stimulates lymphopoietic development and differentiation. Thus, the utilities asserted in the '318 application are specific, substantial and credible.

In certain aspects, the instant case is similar to *Ex parte Hedrick*, Bd. Pat. App. Int. September 22, 2005 (unpublished, copy enclosed). In *Ex parte Hedrick*, the claims are directed to binding compounds that recognize a novel interleukin, IL-1δ. The Board of Patent Appeals and Interferences held that the utility requirement is satisfied "because the evidence of record shows that the disclosed interleukin is likely to be involved in inflammation." *Id.* at page 1. Specifically, Hedrick's application discloses that IL-1δ sequence is similar to the sequences of other IL-1 family members, and that all known IL-1 family members play a role in inflammation. Hedrick's specification asserts that IL-1δ "likely play[s] a role in modulating of local and

systemic inflammatory processes," and post-filing evidence confirms this assertion. Against the Examiner's rejection on the ground that Hedrick's specification does not disclose whether IL-1δ contributes to or inhibits inflammation, the Board held that the binding compounds have utilities either way:

> Once it has been accepted that IL-1δ either contributes to or inhibits the inflammatory response, it seems that those skilled in the art would recognize the claimed binding compounds as useful. Specifically, if IL-1δ contributes to inflammation, those skilled in the art would recognize the claimed compounds to be useful in inhibiting inflammation. On the other hand, if IL-1δ inhibits inflammation, those skilled in the art would recognize the claimed compounds to be useful in promoting inflammation. *Id.* at page 10.

In the instant case, IL-B50 is structurally similar to IL-7, which is known to stimulate lymphopoietic development and differentiation. The '318 application asserts that IL-B50 and IL-7 likely share similar biological activities, and this assertion is confirmed by the data presented in the present application. Thus, the asserted utilities in this case are more specific than, while equally substantial and credible as, those in *Ex parte Hedrick*. Since the binding compounds in *Ex parte Hedrick* are deemed to have patentable utility, the '318 application also adequately supports patentable utility of the binding compounds of the present application.

Accordingly, the '318 application satisfies the utility requirement, and the claimed invention is entitled to the benefit of the filing date of the '318 application, namely September 21, 1998.

Rejections Under 35 U.S.C. §112, Second Paragraph (Paragraph 8 of the Office Action)

The rejection of claim 40 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention, is respectfully traversed for the reasons set forth below.

Claim 40 is directed to the detection kit of claim 36 further comprising a means for separating bound binding compounds from free binding compounds. The Office Action asserts that no function is specified:

> The word "means" is preceded by the word(s) "comprising a" in an attempt to use a "means" clause to recite a claim element as a means for performing a specified function.

> However, since no function is specified by the word(s) preceding "means," it is impossible to determine the equivalents of the element, as required by 35 U.S.C. 112, sixth paragraph. See *Ex parte Klumb*, 159 USPQ 694 (Bd. App. 1967).

Applicants are confused by this rejection. Claim 40 recites "a means for separating bound binding compounds from free binding compounds," thus the function of the means is clearly specified as "separating bound binding compounds from free binding compounds." Applicants are not aware of a requirement under 35 U.S.C. §112, sixth paragraph, that the function of a means has to precede the word "means" in the claim. In fact, the case cited by the Office Action, *Ex parte Klumb*, explicitly states "we see no necessity for construing the statute to require a particular grammatic construction... Thus, expressions, such as 'means for printing' or 'printing means', would have the same connotations and both would be in conformity with the statute." *Id.* at 695.

Accordingly, withdrawal of this rejection is respectfully requested.

Rejections Under 35 U.S.C. §112, Written Description (Paragraph 9 of the Office Action)

The rejection of claims 21-40 under 35 U.S.C. §112, first paragraph, as allegedly containing new matter, is respectfully traversed for the reasons set forth below. Points A) through E) of the Office Action are discussed in turn. Applicants are not addressing the remarks regarding a preliminary amendment filed March 15, 2002 and claims 43, 44 and 46, since there is no such preliminary amendment (the present application was filed on June 20, 2003) or claims (claims 21-40 are pending).

A) An isolated binding compound that specifically binds a polypeptide consisting of SEQ ID NO:2 (claim 2)

In addition to the original claims, support for this claim can be found, for example, at page 7, lines 20-22 and page 6, lines 22-25:

> In binding compound embodiments, the compound may have an antigen binding site from an antibody, which specifically binds to a natural IL-B50 polypeptide (page 7, lines 20-22)

> In various protein embodiments, the invention provides: a substantially pure or recombinant IL-B50 polypeptide exhibiting identity over a length of at least about 12 amino acids to SEQ ID NO: 2 or 4; a natural sequence IL-B50 of SEQ ID NO: 2 or 4 (page 6, lines 22-25).

The Office Action states that the claimed invention is much broader than the original claim "which is limited to a binding site of an antibody and not the entire binding compound." Applicants wish to point out that the original claims are directed to binding compounds but not binding sites (see, for example, original claims 11 and 12).

B) The binding compound that is a neutralizing antibody (claim 27)

The Office Action states that page 24, lines 20-21 of the specification "mentions usefulness of neutralizing antibodies but does not mention the binding compound to be a neutralizing compound." However, in order to comply with the written description requirement, the specification "need not describe the claimed subject matter in exactly the same terms as used in the claims; it must simply indicate to persons skilled in the art that as of the [filing] date the applicant had invented what is now claimed." *All Dental Prodx LLC v. Advantage Dental Products Inc.*, 64 USPQ2d 1945, 1948 (Fed. Cir. 2002). Literal support is not required under the first paragraph of 35 U.S.C. 112; it is required that the originally-filed disclosure would have conveyed to one having ordinary skill in the art that the inventors had possession of the concept of the claimed invention. *Ex parte Parks*, 30 USPQ2d 1234 (Bd. Pat. App. Int. 1993). In the present case, it is clear that a binding compound can be an antibody (see, *e.g.*, original claim 12 b) 1), original claim 14, or page 7, lines 20-30). The specification also discloses that the antibody of this application can be a neutralizing antibody (page 24, lines 17-21):

> The antibodies of this invention can also be useful in diagnostic applications. As capture or non-neutralizing antibodies, they can be screened for ability to bind to the antigens without inhibiting binding to a receptor. As neutralizing antibodies, they can be useful in competitive binding assays.

Therefore, the specification sufficiently indicates to skilled artisans that a binding compound of the present application can be a neutralizing antibody.

C) The binding compound is raised against a purified or recombinantly produced polypeptide comprising SEQ ID NO:2 (claim 31), raised against an antigen comprising at least 8 contiguous amino acids (claim 32), or raised against an antigen comprising at least 12 contiguous amino acids (claim 33) from SEQ ID NO:2.

The Office Action questions about the support for a binding compound raised against a purified or recombinantly produced polypeptide. Support can be found, for example, at page 27, lines 3-4 and page 22, lines 12-14:

> The purified protein or defined peptides are useful for generating antibodies by standard methods, as described above. (page 27, lines 3-4; emphasis added)
>
> Antibodies can be raised to various epitopes of the IL B50 proteins, including species, polymorphic, or allelic variants, and fragments thereof, both in their naturally occurring forms and in their recombinant forms. (page 22, lines 12-14; emphasis added)

With respect to claims 32 and 33, the Office Action seems to allege that the specification supports the recitation "at least about 8" but not "at least 8" contiguous amino acids. As discussed above, written description does not require literal support; what is required is that the originally-filed disclosure would have conveyed to one having ordinary skill in the art that the inventors had possession of the concept of the claimed invention. Pursuant to MPEP 2163.05 III, with respect to changing numerical range limitations, the analysis must take into account which ranges one skilled in the art would consider inherently supported by the discussion in the original disclosure. Here, "at least 8" is inherently supported by "at least about 8, " as a skilled artisan would immediately recognize that "at least 8" is encompassed by "at least about 8," and that the inventors had possession of the concept of a fragment of at least 8 contiguous amino acids. Therefore, no new matter has been introduced.

D) The antigen comprises the at least 8 contiguous amino acids from SEQ ID NO:2 conjugated to an immunogenic protein (claim 35)

The Office Action states that page 22, lines 18-21 of the specification mentions that antibodies can be raised by immunization of animals with conjugates of the fragments with immunogenic

proteins, but it does not mention that the antigen comprises at least 8 contiguous amino acids from SEQ ID NO:2 conjugated to an immunogenic protein.

As the Office Action correctly points out, the specification discloses that antibodies can be raised by immunization with conjugates of fragments with immunogenic proteins. This disclosure is consistent with the notion that fragments of IL-B50 can be used as immunogen:

> A solubilized IL-B50 or fragment of this invention can be used as an immunogen for the production of antisera or antibodies specific for binding. (page 20, lines 16-17)
>
> Antibodies, including binding fragments and single chain versions, against predetermined fragments of the antigens can be raised by immunization of animals with conjugates of the fragments with immunogenic proteins. (page 22, lines 18-21)

Furthermore, fragments, as disclosed in the specification, include a stretch of amino acid residues of at least about 8 amino acids, at least about 12 amino acids, at least about 16 amino acids, and so on:

> The term "polypeptide" as used herein includes a significant fragment or segment, and encompasses a stretch of amino acid residues of at least about 8 amino acids, generally at least about 12 amino acids, typically at least about 16 amino acids, preferably at least about 20 amino acids, and, in particularly preferred embodiments, at least about 30 or more amino acids, e.g., 35, 40, 45, 50, etc. Such fragments may have ends which begin and/or end at virtually all positions... (page 13, lines 10-16)

Therefore, the specification clearly conveys to a person of ordinary skill in the art that a fragment may include at least about 8 amino acids or at least about 12 amino acids from the IL-B50 sequence, and such a fragment can be conjugated with an immunogenic protein to raise antibodies. As discussed above, "at least 8" is inherently supported by "at least about 8," thus the specification also supports conjugating fragments that include at least 8, 12, etc. amino acids. Accordingly, the claims at issue do not contain new matter.

E) The detection kit, wherein the detection is performed using enzyme-linked immunosorbent assay (ELISA) (claim 39)

As disclosed at page 42, line 29 to page 43, line 24 of the specification, antibodies can be used in various diagnostic assays (including ELISA and all the assays recited in claim 39), and the reagents of the diagnostic assays can be supplied in kits:

> Antibodies, including antigen binding fragments, specific for the IL-B50 or fragments are useful in diagnostic applications to detect the presence of elevated levels of IL-B50 and/or its fragments. Such diagnostic assays can employ lysates, live cells, fixed cells, immunofluorescence, cell cultures, body fluids, and further can involve the detection of antigens related to the antigen in serum, or the like. Diagnostic assays may be homogeneous (without a separation step between free reagent and antigen-binding partner complex) or heterogeneous (with a separation step). Various commercial assays exist, such as radioimmunoassay (RIA), enzyme-linked immunosorbent assay (ELISA), enzyme immunoassay (EIA), enzyme-multiplied immunoassay technique (EMIT), substrate-labeled fluorescent immunoassay (SLFIA), and the like. See, e.g., Van Vunakis, et al. (1980) Meth Enzymol. 70:1-525; Harlow and Lane (1980) Antibodies: A Laboratory Manual, CSH Press, NY; and Coligan, et al. (eds. 1993) Current Protocols in Immunology, Greene and Wiley, NY.
>
> Anti-idiotypic antibodies may have similar use to diagnose presence of antibodies against an IL-B50, as such may be diagnostic of various abnormal states. For example, overproduction of IL-B50 may result in production of various immunological reactions which may be diagnostic of abnormal physiological states, particularly in proliferative cell conditions such as cancer or abnormal activation or differentiation. Moreover, the distribution pattern available provides information that the cytokine is expressed in pancreatic islets, suggesting the possibility that the cytokine may be involved in function of that organ, e.g., in a diabetes relevant medical condition.
>
> Frequently, the reagents for diagnostic assays are supplied in kits, so as to optimize the sensitivity of the assay. (page 42, line 29 to page 43, line 24).

Thus, the detection kit of claim 39 is sufficiently supported.

In view of the above, withdrawal of this rejection is respectfully requested.

Rejections Under 35 U.S.C. §§102 and 103 (Paragraphs 10-13 of the Office Action)

The rejections of various claims under 35 U.S.C. §102 as allegedly unpatentable in view of U.S. Patent No. 6,555,520 (hereinafter "the '520 patent"), or under 35 U.S.C. §103 as allegedly unpatentable in view of the combination of the '520 patent and other cited references, are respectfully traversed for the reasons set forth below.

As discussed above, the present claims are entitled to the benefit of the filing date of the '318 application, filed September 21, 1998. Since the '520 patent was filed on May 9, 2001, with an earliest possible priority date of November 13, 1998, it is not prior art with respect to the claimed invention. Therefore, withdrawal of these rejections is respectfully requested.

Conclusions

For the reasons set forth above, Applicants submit that the claims of this application are patentable. Reconsideration and withdrawal of the Examiner's objections and rejections are hereby requested.

In the event that a telephone conversation could expedite the prosecution of this application, the Examiner is requested to call the undersigned at (650) 839-5044.

Please apply any charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: Feb. 3, 2006

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